

### **REMARKS**

Claims 26-30 have been amended and new claim 31 has been added. No new subject matter is believed to have been added. Support for the present amendments can be found in Example 5 on pages 99-103 of the specification.

#### **Rejection under 35 USC 112 first and second paragraph**

Applicants believe it would be helpful to summarize the important features of the present claimed invention.

The end point of an assay to determine whether a transposition reaction has been stopped is to measure the number of transformants.

It has previously been shown that raising the temperature of the transposition reaction mixture to 65°C was not effective in producing transformants. At the time of the invention, persons of ordinary skill in the art assumed that since a temperature of 65°C did not stop the transposon reaction, no change in temperature would be effective for this purpose.

Furthermore it was known that stopping the reaction by adding ethanol was also not successful. A standard method for stopping a transposition reaction was to use a phenol/chloroform extraction (to stop the reaction) and ethanol precipitation (to clean up the DNA and purify it away from toxic phenol). This however was not desirable because of difficulties in removing these organic solvents and loss of DNA during manipulation.

Applicants surprisingly discovered for the first time that raising the temperature above 65°C was just as effective in stopping a

reaction as using the phenol chloroform mixture and much more desirable because of the speed, accuracy and absence of contaminating organic solvent. In the particular example, applicants described the effects of raising the temperature to 75°C. This description in which 75°C is shown to be capable of disrupting a DNA-protein complex inherently teaches to one of ordinary skill in the art that a temperature of greater than 65°C is effective up to the denaturation temperature of DNA.

Any person of ordinary skill in the art of biochemistry will appreciate that there is no single temperature at which protein denaturation exclusively occurs. Instead, protein denaturation kinetics follow a statistical normal distribution in which the preferred temperature occurs at the peak of the bell curve and temperatures close to the preferred temperature will be almost as effective. Based on the results presented on page 103, table 9 and Figure 14, it would be an inherent property that any temperature within the range from at least 5°C below the preferred temperature to the denaturation temperature of DNA would be effective in the claimed method. To limit the claimed invention to a single temperature would invite copyists and would not be proper reward to the inventor for their useful invention in which organic solvents can be replaced by a temperature shift.

Moreover, while applicants described the results in Table 9 on page 103 for 75°C, the method for testing the effects of raising the temperature higher than 65°C are described in Example 5 in such a manner as to easily permit a person of ordinary skill in the art to determine the effectiveness of that temperature on stopping the transposon reaction without undue experimentation.

The assay provided in claim 5 together with Table 9 on page 103 describes what is an effective time for achieving a stop treatment that results in a satisfactory number of transformants.

(a) The absence of a period is objected to in claim 26. This punctuation has been added.

(b) The phrase "suitable for transforming a host cell" (emphasis added) is objected to. The examiner asserts that this is new subject matter and furthermore that it is indefinite and not enabled. Applicants have amended the claim language so as to remove the term "suitable".

(c) The term " processing occurs in the absence of a phenol extraction step". (emphasis added). The Examiner asserts that a specific instruction is required and not a negative limitation. The claims has been amended to remove negative limitations.

(d) The Examiner asserts that the specification is enabled "for a method for subjecting DNA to a temperature of 75°C but not to 65°C to disrupt a complex of target DNA, donor DNA and a transposase in an in vitro transposition assay."

The applicants respectfully disagree. As discussed above, the invention relates to increasing the temperature to stop the transposon reaction. Whereas 65°C was not effective, 75°C was highly effective. It is well known that protein unfolding is not limited to a precise temperature. Moreover, it would be well within the expertise of one of ordinary skill in the art to use the assay described in Example 5 on pages 99-103 at any temperature higher than 65°C to stop the transposon reaction. To require applicants to limit the claims to 75°C would be to invite copyists to modify slightly the temperature specified and to readily exploit applicant's invention by replacing organic

solvents by increasing the temperature above 65°C while avoiding the single specified temperature.

(e) The examiner objects to the term "effective" as indefinite with respect to an amount of time. Although applicants believe this term to be clear in meaning, claim 26 has been amended to remove this term.

Rejection under 35 USC 102f

Applicants enclose herewith a Petition to amend inventorship, and a Fee for adding inventors hitherto un-named according to 37C.F.R. 1.48(n) in a non-provisional application.

The present claims are different from those originally filed. The originally filed claims properly identified Nancy Craig as the inventor. The present divisional application contains new claims based on subject matter in the specification, where the inventors for these new claims are Lise Raleigh and Fiona Stewart in addition to Nancy Craig. Upon acceptance of the petition, the inventorship will be Nancy Craig, Elisabeth Raleigh and Fiona Stewart.

In view of the presently submitted petition, the Examiner is respectfully requested to reverse this rejection.

### **CONCLUSION**

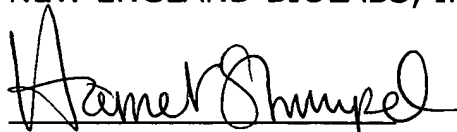
For the reasons set forth above, Applicants respectfully submit that the rejections set forth in the Official Action of November 3, 2003 have been overcome and that this case is in condition for immediate allowance. Early and favorable consideration leading to prompt issuance of this Application is earnestly solicited.

Applicants hereby petition for a three-month extension of time to file the response to the office action dated November 3, 2003. A check in the amount of \$685 is enclosed, covering the \$475 extension fee, the \$130 fee for Amendment to Add Erroneously Not Named Inventors to Application and \$80 for two Requests for Recordation of Assignment. If any additional fee is required, please charge amount to Deposit Account No. 14-0740.

Should the Examiner wish to discuss any of the amendments and/or remarks made herein, the undersigned Attorney would appreciate the opportunity to do so.

Date: April 21, 2004

Respectfully submitted,  
NEW ENGLAND BIOLABS, INC.

A handwritten signature in black ink, appearing to read "Harriet Strimpel", written over a horizontal line.

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